CLAIMS

1. A detection method for intracellular integrase activity using a promoterless reporter gene.

2. The detection method according to claim 1, wherein the reporter gene may be luciferase, GFP or an antibiotic selection marker.

3. The detection method according to claim 1 or 2, wherein a reporter gene construct is generated from the reporter gene and the construct is used as the substrate of the enzymatically active retroviral protein expressed from the synthetic gene in accordance with claims 17 to 26.

4. Packaging construct for a lentiviral or complex retroviral vector based on a synthetic *gag* or *pol* gene.

5. Packaging construct according to claim 4, wherein the synthetic gene is the synthetic gene in accordance with any of claims 17 to 26.

6. A method of transfecting a eukaryotic cell using the expression vector in accordance with any of claims 27 to 29.

7. A eukaryotic cell line harboring the synthetic gene or region of a gene in accordance with any of the claims 17 to 26.

8. The eukaryotic cell line according to claim 7, wherein the retroviral enzymatically active protein is expressed using a constitutive, inducable or tissue specific promoter.

9. The eukaryotic cell line according to claim 7 or 8, wherein the expression is stable.

10. A transgenic, non-human, animal harboring the synthetic gene or region of a gene in accordance with claims 17 to 26.

11. The transgenic animal according to claim 10, wherein the expression of the synthetic gene or region of a gene is induced by an inducable promoter or by a tissue-specific promoter.

12. The transgenic animal according to claim 10 or 11, wherein the animal is a mammal.

13. A method for preparing a synthetic gene or region of a gene encoding a retroviral protein or part of such a protein which is enzymatically active in a target eukaryotic cell, comprising the steps of:

1) identifying a group of genes from the total set of genes of the target eukaryotic cell which encode proteins which are naturally expressed easily and/or in high concentrations in the target cell;

2) determining the codon sequences of these identified genes and from these sequences a preferred codon usage and a preferred nucleotide pair frequency;

3) using the preferred codon usage, identify the non-preferred codons in the natural gene encoding the enzymatically active protein;

4) replacing one or more of the non-preferred codons with one or more preferred codons encoding the same amino acids as the replaced codons while biasing the replacement to obtain the preferred nucleotide pair frequency.

14. The method according to claim 13, wherein the replacement step is carried out based on a random choice between alternative codons encoding the same amino acid at each position using a random number generator and biasing the choice of alternative codons based on the preferred codon usage to obtain the preferred nucleotide pair frequency.

15. A method for gene transfer in a eukaryotic cell expressing the synthetic gene or region of the gene in accordance with any of the claims 17 to 26.

16. A method according to claim 15, wherein the synthetic gene is transiently expressed or is stably integrated in said cell.

17. A synthetic retroviral *gag* or *pol* gene or a region of a retroviral *gag* or *pol* gene for the expression of a retroviral *gag* or *pol* protein in a eukaryotic cell, the expressed retroviral protein being expressed at a level to provide detectable activity of the wild-type

function of the expressed retroviral protein in the eukaryotic cell.

18. The synthetic gene according to claim 17, wherein the retroviral genes have non-preferred codons when referred to the eukaryotic cell, the number of non-preferred codons being such that replacement of all the non-preferred codons by preferred codons with respect to the eukaryotic cell results in a GC nucleotide pair content of 65% or higher, the synthetic gene having a GC nucleotide pair content of between 53 and 63%, more preferably between 55 and 61% and the expressed retroviral protein is expressed at a level to provide detectable enzymatic activity of the expressed retroviral protein in the eukaryotic cell.

19. The synthetic gene according to claim 17 or 18, wherein the expression of the gag or pol proteins is independent of retroviral regulatory proteins.

20. The synthetic gene according to any of the claims 17 to 19, wherein the retroviral protein is a lentiviral gag or pol protein.

21. The synthetic gene according to claim 20, wherein the lentiviral protein is an HIV gag or pol protein.

22. The synthetic gene according to any of claims 18 to 21, wherein the detectable activity of the enzymatic function includes at least promotion or stimulation of the integration of DNA fragments into the host cell DNA, preferably the chromosome of the host cell.

23. The synthetic gene according to any of claims 17 to 22, wherein the retroviral protein is a protease, reverse transcriptase, integrase protein or a polyprotein gag-pol precursor thereof.

24. The synthetic gene according to any of the claims 17 to 23, wherein the eukaryotic cell is a mammalian cell.

25. The synthetic gene according to any of the claims 17 to 24, wherein the expression of

the protein is at a level of at least 200% of that expressed by the wild type gene in the eukaryotic cell.

26. The synthetic gene according to any of the claims 17 to 25, comprising the sequence of Fig. 2A or homologs thereof which have a GC content between 53 and 63%, preferably between 55 and 61%.

27. A eukaryotic expression vector comprising the synthetic gene or region of a gene in accordance with any of the claims 17 to 26.

28. The expression vector according to claim 27, further comprising a constitutive or an inducible or a tissue-specific promoter.

29. The expression vector according to claim 27 or 28, comprising a plasmid, a mammalian or an insect virus.